In re Application of: Casterman et al.

Application No.: 10/751,826

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1-17. (cancelled)

- 18. (new) An immunoglobulin or a fragment thereof, that specifically binds an antigen of interest, wherein said immunoglobulin or said fragment thereof comprises a variable region of a heavy polypeptide chain said variable region being devoid of normal light chain interaction sites.
- 19. (new) An immunoglobulin or a fragment thereof, that specifically binds an antigen of interest, wherein said immunoglobulin or said fragment thereof comprises at least part of the variable region of a heavy polypeptide chain said variable region being devoid of normal light chain interaction sites and wherein the immunoglobulin is a heavy-chain immunoglobulin.
- 20. (new) A fragment of an immunoglobulin according to claim 18, which is the variable region of the heavy chain of said immunoglobulin.
- 21. (new) A fragment of an immunoglobulin according to claim 19, which is the variable region of the heavy chain of said immunoglobulin.
- 22. (new) An immunoglobulin or a fragment thereof according to claim 19, which has a constant region which is devoid of CH1 domain.
- 23. (new) A fragment of an immunoglobulin according to claim 18 which is combined with a fragment of a four-chain immunoglobulin.
- 24. (new) A fragment of an immunoglobulin according to claim 19, which is combined with a fragment of a four-chain immunoglobulin.

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25. (new) A fragment of an immunoglobulin according to claim 18, which is expressed in a prokaryotic or in a eukaryotic host cell.

- 26. (new) A fragment of an immunoglobulin according to claim 19, which is expressed in a prokaryotic or in a eukaryotic host cell.
- 27. (new) A fragment of an immunoglobulin according to claim 21, which is expressed in a prokaryotic or in a eukaryotic host cell.
- 28. (new) A fragment of an immunoglobulin according to claim 19, which comprises at least 10 amino acid residues of the variable region of a heavy polypeptide chain and comprises the residue corresponding to position 45 in the immunoglobulin said residue at position 45 being a charged amino acid residue or a cysteine residue.
- 29. (new) A fragment of an immunoglobulin according to claim 28, which is combined with a fragment of a four-chain immunoglobulin.
- 30. (new) A modified 4-chain immunoglobulin or a fragment thereof comprising a variable VH region which is modified such that the VH region has been partially replaced by specific sequences or amino acid residues of an immunoglobulin according to claim 19.
- 31. (new) The immunoglobulin or a fragment thereof according to claim 18 or 19, wherein the immunoglobulin or fragment is suitable for use in *in vitro* diagnosis.
- 32. (new) The immunoglobulin or a fragment thereof according to claim 18 or 19, wherein the immunoglobulin or fragment is suitable for use in *in vivo* diagnosis.
- 33. (new) The immunoglobulin or a fragment thereof according to claim 18 or 19, which is labelled with a detectable label.

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- 34. (new) The immunoglobulin or a fragment thereof according to claim 33, wherein the detectable label is an imaging agent.
- 35. (new) The immunoglobulin or a fragment thereof according to claim 33, wherein the detectable label is selected from the group consisting of a radio isotope, a chemical marker, an enzymatic marker, or a chemiluminescent marker.
- 36. (new) An immunoglobulin or a fragment thereof according to claim 18 or 19, which is directed against an immunoglobulin idiotype.
- 37. (new) A method for detecting the presence of a bacterium, virus, or parasite in a biological sample, comprising the steps of:
 - (a) contacting the biological sample with the immunoglobulin according to claim18 or 19 that specifically binds said bacterium, virus, or parasite; and
 - (b) detecting binding of the immunoglobulin or fragment.
- 38. (new) The method according to claim 37, wherein the virus is HIV or hepatitis B virus.
- 39. (new) A method for detecting the presence of a tumor in a biological sample, comprising the steps of:
 - (a) contacting the biological sample with the immunoglobulin according to claim18 or 19 that specifically binds a protein present on said tumor; and
 - (b) detecting binding of the immunoglobulin or fragment.
- 40. (new) A method for detecting the presence of myeloma in a biological sample, comprising the steps of:
 - (a) contacting the biological sample with the immunoglobulin according to claim18 or 19 that specifically binds a myeloma immunoglobulin epitope; and

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- (b) detecting binding of the immunoglobulin or fragment.
- 41. (new) A method for detecting a biological molecule in a biological sample, comprising the steps of:
 - (a) contacting the biological sample with the immunoglobulin according to claim 18 or 19 that specifically binds said biological molecule; and
 - (b) detecting binding of the immunoglobulin or fragment.
- 42. (new) The method according to claim 41, wherein said biological molecule is a protein, viral envelope glycoprotein, hapten, carbohydrate, nucleic acid, cellulare receptor, or a membrane protein.
- 43. (new) The method according to claim 42, wherein the biological molecule is galactosyl α -1,3-galactose, a myeloma immunoglobulin epitope, or a hepatitis B surface antigen.
- 44. (new) A method for detecting the presence of a bacterium, virus, or parasite in a subject, comprising the steps of:
 - (a) administering to the subject the immunoglobulin according to claim 18 or 19 that specifically binds said bacterium, virus, or parasite; and
 - (b) detecting binding of the immunoglobulin or fragment.
- 45. (new) The method according to claim 37, wherein the virus is HIV or hepatitis B virus.
- 46. (new) A method for detecting the presence of a tumor in subject, comprising the steps of (a) administering to the subject the immunoglobulin according to claim 18 or 19 that specifically binds a protein present on said tumor, and (b) detecting binding of the immunoglobulin or fragment.

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47. (new) A method for detecting the presence of myeloma in a subject, comprising the steps of:

- (a) administering to the subject the immunoglobulin according to claim 18 or 19 that specifically binds a myeloma immunoglobulin epitope; and
- (b) detecting binding of the immunoglobulin or fragment.
- 48. (new) A method for detecting a biological molecule in a subject, comprising the steps of:
 - (a) administering to the subject the immunoglobulin according to claim 18 or 19 that specifically binds said biological molecule; and
 - (b) detecting binding of the immunoglobulin or fragment.
- 49. (new) The method according to claim 41, wherein said biological molecule is a protein, viral envelope glycoprotein, hapten, carbohydrate, nucleic acid, cellulare receptor, or a membrane protein.
- 50. (new) The method according to claim 42, wherein the biological molecule is galactosyl α -1,3-galactose, a myeloma immunoglobulin epitope, or a hepatitis B surface antigen.
- 51. (new) A composition comprising an immunoglobulin or a fragment thereof that specifically binds to an antigen of interest, wherein said immunoglobulin comprises a variable region of a heavy polypeptide chain, said variable region being devoid of normal light chain interaction sites.
- 52. (new) A composition comprising an immunoglobulin or a fragment thereof that specifically binds to an antigen of interest, wherein said immunoglobulin comprises at least part of the variable region of a heavy polypeptide chain, said variable region

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being devoid of normal light chain interaction sites and wherein the immunoglobulin is a heavy-chain immunoglobulin.

- 53. (new) The composition according to claim 51 or 52, wherein the immunoglobulin or fragment specifically binds a protein, hapten, carbohydrate or nucleic acid.
- 54. (new) The composition according to claim 51 or 52, wherein the immunoglobulin or fragment specifically binds a protein present on tumor cells.
- 55. (new) The composition according to claim 51 or 52, wherein the immunoglobulin or fragment thereof is combined with a toxin, enzyme, drug, hormone, or cytokine.
- 56. (new) The composition according to claim 54, wherein the toxin is mistletoe lectin toxin.
- 57. (new) The composition according to claim 51 or 52, wherein the immunoglobulin or fragment thereof is bifunctional or multifunctional.
- 58. (new) The composition according to claims 51 or 52, wherein the immunoglobulin or fragment thereof is heterospecific.
- 59. (new) The composition according to claim 58, wherein the immunoglobulin or fragment thereof is capable of targeting drugs, hormones or cytokines to cells.
- 60. (new) A method of treating cancer in a mammal, comprising the step of administering the composition according to claim 51 or 52, wherein the immunoglobulin or fragment thereof specifically binds to a tumor-specific protein.
- 61. (new) A method of inducing protection against a pathological agent in a mammal, comprising the step of administering the composition according to claim 51 or

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52, wherein the immunoglobulin or fragment thereof specifically binds to the pathological agent.

- 62. (new) A method of regulating the expression or the activity of a protein in a mammal, comprising the step of administering the composition according to claim 51 or 52, wherein the immunoglobulin or fragment thereof binds to said protein.
- 63. (new) A method of modifying the metaboloism of a cell comprising the step of administering an immunoglobulin or a fragment thereof according to claim 18 or 19.